

2



# THE OREGON HEALTH SCIENCES UNIVERSITY

3181 S.W. Sam Jackson Park Road, L333A, Portland, Oregon 97201, (503) [REDACTED] FAX 494-8393

494-8414 494-4430

*School of Medicine  
Dept. of Biochemistry*

# DTIC

## AD-A235 910



May 5, 1991

Dr. Steve Lewis  
Office of Naval Research  
Combat Casualty Care Research Area  
Naval Medical Research & Development Command  
Naval Medical Command, National Capitol Region  
Code 405  
Bethesda, MD 20814-5044

Subject: Quarterly Report for Award N00014-90-J1797  
Liquid Collagen Wound Coverings

Dear Dr. Lewis:

Attached is a brief summary of research progress since our last report of December 10, 1990. As you will recall you had earlier recommended that I adopt a four monthly reporting schedule, rather than a quarterly reporting schedule.

Yours sincerely,

J. Peter Bentley, PhD  
Professor of Biochemistry  
and Molecular Biology

cc: Administrative Grants Officer  
Director, Naval Research Laboratory  
Defense Technical Information Center  
Office of Chief of Naval Operations  
Bureau of Medicine and Surgery

FILE COPY

*Schools:*  
Schools of Dentistry, Medicine, Nursing

*Clinical Facilities:*  
University Hospital  
Doernbecher Memorial Hospital for Children  
Crippled Children's Division  
Outpatient Clinics

*Special Research Division:*  
Institute for Advanced Biomedical Research

Accession For	
NTIS GRA&I	<input checked="" type="checkbox"/>
DTIC TAB	<input type="checkbox"/>
Unannounced	<input type="checkbox"/>
Justification	
by Rec A230 390	
Distribution/	
Availability Codes	
Avail and/or	
Special	
A-1	

**Liquid Collagen Wound Coverings Award Number N00014-90-J1797 Quarterly Report  
May 5, 1991**

**Introduction**

Captain Steven Lewis, MD, visited the laboratory in March, 1991, and met with all of the staff to discuss progress on this project. In addition, he met with Alan Seyfer, MD, Professor of Surgery, Chief of Plastic and Reconstructive Surgery, to discuss future projects of interest.

**Collagen Preparation**

Since the last report on December 10, two additional batches of collagen have been prepared and microbiological studies carried out with a contract laboratory (Consulting Clinical Microbiological Labs, Portland, Oregon). The last two batches have proved to be sterile after culture for seven days in several different kinds of medium. We have modified our storage procedure and the recent batches are now stored in 0.01 M HCL at liquid nitrogen temperatures, which simplifies the reconstitution when the batches are to be used.

**Sterilization of Collagen Preparations**

In an attempt to overcome the fragmentation produced when freeze dried collagen preparations are subjected to gamma irradiation, we have added DOPA at a concentration of  $10^{-3}$  M prior to freeze drying. These preparations were subsequently exposed to varying amounts of gamma irradiation up to 2.5 megarads. Dramatic stabilization of the collagen was seen after the addition of DOPA. We propose this is because DOPA acts as a free radical sink and thus protects against free radical damage induced by the radiation. To extend this study we have recently exposed collagen preparations to gamma irradiation after the addition of other free radical sinks, hypotaurine and taurine (as a control). Initial polyacrylamide gel studies show similar protection to that earlier noted with DOPA. These studies are ongoing.

**Covalent Binding of DOPA**

The experiments attempting to covalently bind a crosslinking agent (L-DOPA) to collagen by activating either the collagen or the DOPA with EDAC are continuing with no major progress to report at this time.

**Human Studies**

We have currently enrolled six additional patients with split thickness skin graft donor sites in the clinical trials of our collagen pourable wound dressing. All patients have tolerated the application well and there have been no adverse reactions noted. In addition, there has been no incidence of infection.

91 5 13 008

We have expanded the study group to include more complicated wounds, i.e. venous stasis ulcers and partial thickness burns. These wounds are an obvious next step in the evaluation of any topical wound therapy and offer the additional advantage of providing more objective data for comparison. Addenda have been submitted to the human use committee at OHSU and at the Portland VA Medical Center to include these wounds. In addition, we have contacted Dr. Phillip Parshley, Chief of the burn unit at Emanuel Hospital. He will likely be collaborating with us, which should vastly increase our patient population in the near future.

#### Vehicle for Growth Factors

Our studies using collagen as a delivery vehicle for growth factors are underway. Initial results using collagen ring implants, crosslinked with DOPA, implanted subpectorally in rats, reveal that they are present and maintain their shape for at least 28 days. Previous experience has shown that we see osteogenesis after 28 days with osteogenin provided it is in a vehicle which "holds it in place." Others have had similar observations using PDGF and TGF-b, i.e., that the longer it is maintained in proximity, the more effective it is. The fact that dopacol is not degraded in this period and that it can theoretically be incorporated by the native tissues, encourages its use as a delivery vehicle.

We are now beginning a trial with osteogenin/dopacol implants and will soon be looking at topical application of PDGF/collagen as a pseudodermis.